UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,636	02/25/2002	Ulrich Noth	00325-052901	3647

26248 7590 08/09/2004

NIXON PEABODY LLP
101 FEDERAL ST
BOSTON, MA 02110

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,636	NOTH ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ___.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 05/27/04 has been acknowledged.

Claims 1-10 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-4, 7-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Caplan et al (US 5,486,359 1996), for the same reasons of record as set forth in the office action mailed on 02/25/04.

The instant claims are drawn to an isolated population of mesenchymal stem cells and a pharmaceutical composition thereof which can differentiate into cells of more than one connective tissue type (bone, cartilage, adipose, tendon, ligament and dermis) wherein the mesenchymal stem cells are obtained from bone (iliac crest or trabecular bone).

Caplan teaches therapeutic composition comprising an isolated homogeneous population of human mesenchymal stem cells, which can differentiate into cells of more than one connective tissue type (col. 35 claim 1; col. 37 claims 32-38). The cited art teaches that mesenchymal stem cells are the pluripotential blast cells found in bone marrow, blood, dermis and periosteum that are capable of differentiating into any of the specific types of mesenchymal or connective tissues (i.e. the tissues of the body that

support the specialized elements; particularly adipose, osseous, cartilaginous, elastic, and fibrous connective tissues) see col.1 lines 22-34. The cited art further teaches that mesenchymal stem cells can be isolated from the bone marrow obtained firm iliac crest, femora, tibiae, spine, rib or other medullary spaces. Bone marrow is the soft tissue occupying the medullary cavities of long bones, some haversian canals, and spaces between trabeculae of cancellous or spongy bone (col.2 lines 14-21; col.5, lines 10-20).

In addition the cited art clearly anticipate the invention as claimed because the composition and functions as claimed are presumed inherent. The composition is physically the same it must have the same properties. "Products of identical chemical composition can not have mutually exclusive properties."A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) see MPEP § 2112.02. In instant case the mesenchymal stem cells as taught by Caplan are identical to the mesenchymal stem cells as claimed in the instant application, since the prior art clearly teaches "an isolated, homogeneous population of human mesenchymal stem cells, which can differentiate into cells of more than one connective tissue type" see col 35 lines 55-58. Since the mesenchymal stem cells as claimed and in the prior art of record are same, it must have the same properties. Thus the cited art clearly anticipate the invention as claimed.

Response to arguments

The applicant argues that Caplan doess not teach all the elements of the claims. The applicant argues that Caplan teaches mesenchymal stem cells isolated from bone marrow, which is not bone. The present invention is directed to a mesenchymal stem cell population isolated from the mineralized matrix of bone. The applicant argues that this is a surprising and unexpected finding, which is not anticipated by the cited art.

However, applicant's arguments are found NOT persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. a mesenchymal stem cell population isolated from the mineralized matrix of bone) are not recited in the

rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In instant case the invention as claimed is not limited to mesenchymal stem cell population isolated from the mineralized matrix of bone. Thus the given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed.

Claims 1, 5 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerson et al (US 5,591,625, 1997), for the same reasons of record as set forth in the office action mailed on 02/25/04.

The instant claims are drawn to genetically engineered mesenchymal stem cells and a pharmaceutical composition thereof.

Gerson teaches isolated human mesenchymal stem cells, which can differentiate into more than one connective tissue type transfected with exogenous genetic material encoding a protein to be expressed. The cited art teaches the genetic modification of mesenchymal stem cells using a retroviral vector (col.18 lines 43-61; col.20 lines 15-21). In addition the cited art teaches that the scope of genetic modification of mesenchymal stem cells encompasses gene encoding cytokines to enhance hematopoietic reconstitution and the cytokines that promotes repair and healing of injured bones (col. 8, lines 1-67; Col.9 lines 58-67). Thus the cited art clearly anticipate the invention as claimed.

Response to arguments

The applicant argues that Gerson dose not anticipate the instant invention because the bone derived mesenchymal stem cells of the present invention are different than the bone marrow derived stem cells.

However, applicant's arguments are found NOT persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. a mesenchymal stem cell population isolated from the mineralized matrix of bone) are not recited in the

rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In instant case the invention as claimed is not limited to mesenchymal stem cell population isolated from the mineralized matrix of bone. Thus the given the broadest reasonable interpretation the cited art clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gerson et al (US 5591625, 1997) as applied to claims 1,5 and 9 above, and further in view of Breibart et al (US 6077987, 2000).

The instant claims are drawn to genetically engineered mesenchymal stem cells, wherein the genetically engineered cells express a member of transforming growth factor-β superfamily.

Gerson teaches isolated human mesenchymal stem cells, which can differentiate into more than one connective tissue type transfected with exogenous genetic material encoding a protein to be expressed. The cited art teaches the genetic modification of mesenchymal stem cells using a retroviral vector (col. 5-6, col.18 lines 43-61; col.20 lines 15-21). In addition the cited art teaches that the scope of genetic modification of mesenchymal stem cells encompasses cytokines to enhance hematopoietic reconstitution and cytokines that promotes repair and healing of injured bones (col. 8, lines 1-67; Col.9 lines 58-67).

However Gerson does not specifically teach the genetic modification of mesenchymal stem cells to express a member of transforming growth factor-β superfamily.

Breibart teaches genetic modification of mesenchymal cells to express a bioactive molecule selected from the group of TGF-b superfamily in order to promote wound healing, cell proliferation or differentiation in patients. The cited art further

teaches that genetically modified mesenchymal cells are cartilage-forming cell that encodes a bioactive molecule selected from the group of TGF-beta superfamily consisting of bone morphogenic proteins (BMP), TGF-beta, and insulin-like growth factor (IGF). See col.6-7 sec.II, col.14 lines 37-67.

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Gerson who teaches genetic modification of mesenchymal stem cells with Breibart who specifically teaches genetic modification of mesenchymal cells with bone morphogenic proteins (BMP), TGF-beta, and insulin-like growth factor (IGF). One would have been motivated to do so because members of bioactive molecules belonging to TGF-beta superfamily are known to promote wound healing, cell proliferation and/or differentiation. One would have a reasonable expectation of success, since making genetic constructs expressing a bioactive molecule selected from TGF-beta superfamily and transduction of mesenchymal stem cell using a viral or non-viral vectors has been routine in the art at the time of filing. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Response to arguments

The applicant argues that since Gerson dose not teach all limitation (i.e. mesenchymal stem cell population isolated from the mineralized matrix of bone), the invention as claimed is not obvious in view of cited art of record.

However, applicant's arguments are found NOT persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. a mesenchymal stem cell population isolated from the mineralized matrix of bone) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In instant case the invention as claimed is not limited to mesenchymal stem cell population isolated from the mineralized matrix of bone. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to ***(571) 272-0547.***

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image

problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306.**

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
8/5/04